CLAIMS

1. A method of diagnosing a psychosis in a subject, said method comprising the steps of:

(a) analyzing the methylenetetrahydrofolate reductase (MTHFR) nucleic acid in a sample obtained from said subject; and

(b) determining the presence of at least one heterozygous MTHFR mutant allele in said subject, wherein the presence of said mutant allele is indicative of said subject having said psychosis.

2. The method of claim 1, wherein said psychosis is schizophrenia.

3. The method of claim 1, wherein said mutant allele encodes an MTHFR protein with reduced activity or reduced thermal stability.

4. The method of claim 1, wherein said mutant allele comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

5. The method of claim 4, wherein said mutant allele comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

6. A method of determining a risk for a psychosis or propensity thereto in a subject, said method comprising the steps of:

(a) analyzing the MTHFR nucleic acid in a sample obtained from said subject; and

(b) determining the presence of at least one heterozygous MTHFR mutant allele in said subject, wherein the presence of said mutant allele is indicative of a risk for a psychosis or propensity thereto in said subject.

7. The method of claim 6, wherein said psychosis is schizophrenia.

8. The method of claim 6, wherein said mutant allele encodes an MTHFR protein with reduced activity or reduced thermal stability.

9. The method of claim 6, wherein said mutant allele comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at

position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

10. The method of claim 9, wherein said mutant allele comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

11. A method of diagnosing a psychosis in a subject, said method comprising the steps of:

(a) analyzing the MTHFR nucleic acid in a sample obtained from said subject; and

(b) determining the presence of a heterozygous MTHFR mutation at position 677 and the presence of at least one other MTHFR mutation at a position other than 677, wherein the presence of said mutations is indicative of said subject having said psychosis.

12. The method of claim 11, wherein said psychosis is schizophrenia.

13. The method of claim 11, wherein said mutant MTHFR nucleic acid encodes a protein having reduced activity or reduced thermal stability.

14. The method of claim 11, wherein said mutant MTHFR nucleic acid comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764,

a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

15. The method of claim 14, wherein said mutant MTHFR nucleic acid comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

16. A method of diagnosing a risk for a psychosis or propensity thereto in a subject, said method comprising the steps of:

(a) analyzing the MTHFR nucleic acid in a sample obtained from said subject; and

(b) determining the presence of a heterozygous MTHFR mutation at position 677 and the presence of at least one other MTHFR mutation at a position other than 677, wherein the presence of said mutations is indicative of a risk for a psychosis or propensity thereto in said subject.

17. The method of claim 16, wherein said psychosis is schizophrenia.

18. The method of claim 16, wherein said mutant MTHFR nucleic acid encodes a protein having reduced activity or reduced thermal stability.

19. The method of claim 16, wherein said mutant MTHFR nucleic acid comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

20. The method of claim 19, wherein said mutant MTHFR nucleic acid comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

21. A method for stratification of subjects involved in a clinical trial of an anti-psychotic therapy, said method comprising analyzing the MTHFR nucleic acid in a sample obtained from said subject and determining the presence of at least one MTHFR mutant allele in said subject before, during, or after said clinical trial, wherein the presence of said mutant allele in said subject places said subject into a subgroup for said clinical trial.

22. The method of claim 21, wherein said anti-psychotic therapy is a therapy for schizophrenia.

23. The method of claim 21, wherein said mutant allele encodes an MTHFR protein with reduced activity or reduced thermal stability.

24. The method of claim 21, wherein said mutant allele comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

25. The method of claim 24, wherein said mutant allele comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

26. The method of claim 21, wherein said subject comprises at least two MTHFR mutant alleles.

27. The method of claim 26, wherein said mutant alleles comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position

1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

28. The method of claim 27, wherein said mutant alleles comprise at least one of a C/T mutation at position 677 or an A/C mutation at position 1298.

29. A method for selecting a therapy for a subject suffering from a psychosis, said method comprising the steps of:

(a) analyzing the MTHFR nucleic acid in a sample obtained from said subject; and

(b) determining the presence of at least one MTHFR mutant allele in said subject, wherein the presence of said mutant allele is indicative of the safety or efficacy of said therapy.

30. The method of claim 29, wherein said psychosis is schizophrenia.

31. The method of claim 29, wherein said mutant allele encodes an MTHFR protein with reduced activity or reduced thermal stability.

32. The method of claim 29, wherein said mutant allele comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A

mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

33. The method of claim 32, wherein said mutant allele comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

34. The method of claim 29, wherein said subject comprises at least two MTHFR mutant alleles.

35. The method of claim 34, wherein said mutant alleles comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

36. The method of claim 35, wherein said mutant alleles comprise at least one of a C/T mutation at position 677 or an A/C mutation at position 1298.

37. A method for determining whether a mutant MTHFR allele is indicative of a response to a therapy for a psychosis, said method comprises the steps of:

(a) determining whether said response of a first subject or set of subjects at increased risk for or diagnosed with said psychosis differs from said response of a second subject or set of subjects at increased risk for or diagnosed with said psychosis;

(b) analyzing the MTHFR nucleic acid in a sample obtained from said first subject or set of subjects and said second subject or set of subjects; and

(c) determining whether at least one MTHFR mutant allele differs between said first subject or set of subjects and said second subject or set of subjects, wherein the presence of said mutant allele is correlated to said response, thereby determining whether said mutant allele is indicative of the safety or efficacy of said therapy.

38. The method of claim 37, wherein said psychosis is schizophrenia.

39. The method of claim 37, wherein said mutant allele encodes an MTHFR protein with reduced activity or reduced thermal stability.

40. The method of claim 37, wherein said mutant allele comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position

985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

41. The method of claim 40, wherein said mutant allele comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

42. The method of claim 37, wherein said subject comprises at least two MTHFR mutant alleles.

43. The method of claim 42, wherein said mutant alleles comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

44. The method of claim 43, wherein said mutant alleles comprise at least one of a C/T mutation at position 677 or an A/C mutation at position 1298.

45. A method for preventing, delaying, or treating a psychosis in a subject, said method comprising the steps of:

(a) analyzing the MTHFR nucleic acid in a sample obtained from said subject;

(b) determining the presence of at least one MTHFR mutant allele in said subject, wherein the presence of said mutant allele is predictive of the safety or efficacy of at least one anti-psychotic therapy;

(c) determining a preferred therapy for said subject; and

(d) administering said preferred therapy to said subject.

46. The method of claim 45, wherein said psychosis is schizophrenia.

47. The method of claim 45, wherein said mutant allele encodes an MTHFR protein with reduced activity or reduced thermal stability.

48. The method of claim 45, wherein said mutant allele comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

49. The method of claim 48, wherein said mutant allele comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

50. The method of claim 45, wherein said subject comprises at least two MTHFR mutant alleles.

51. The method of claim 50, wherein said mutant alleles comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

52. The method of claim 51, wherein said mutant alleles comprise at least one of a C/T mutation at position 677 or an A/C mutation at position 1298.

53. A pharmaceutical composition comprising

a compound which has a differential effect in subjects having at least one copy of a particular MTHFR allele; and

a pharmaceutically acceptable carrier or excipient or diluent,

wherein said composition is preferentially effective to treat a subject having said MTHFR allele.

54. The method of claim 53, wherein said composition is adapted to be preferentially effective based on the unit dosage, presence of additional active components, complexing of said compound with stabilizing components, or inclusion of components enhancing delivery or slowing excretion of said compound.

55. The composition of claim 53, wherein said compound is deleterious to subjects having at least one said MTHFR allele or in subjects not having at least one said MTHFR allele, but not in both.

56. The composition of claim 53, wherein said subject suffers from a disease or condition selected from the group consisting of amyotrophic lateral sclerosis, anxiety, dementia, depression, epilepsy, Huntington's disease, migraine, demyelinating disease, multiple sclerosis, pain, Parkinson's disease, schizophrenia, psychoses, and stroke.

57. The pharmaceutical composition of claim 53, wherein said composition is subject to a regulatory restriction or recommendation for use of a diagnostic test determining the presence or absence of at least one said MTHFR allele.

58. The pharmaceutical composition of claim 53, wherein said pharmaceutical composition is subject to a regulatory limitation or recommendation restricting or recommending restriction of the use of said pharmaceutical composition to subjects having at least one said MTHFR allele.

59. The pharmaceutical composition of claim 53, wherein said pharmaceutical composition is subject to a regulatory limitation or recommendation indicating said pharmaceutical composition is not to be used in subjects having at least one said MTHFR allele.

60. The pharmaceutical composition of claim 53, wherein said pharmaceutical composition is packaged, and the packaging includes a label or insert restricting or recommending the restriction of the use of said pharmaceutical composition to subjects having at least one said MTHFR allele.

61. The pharmaceutical composition of claim 53, wherein said pharmaceutical composition is packaged, and said packaging includes a label or insert requiring or recommending the use of a test to determine the presence or absence of at least one said MTHFR allele in a subject.

62. The pharmaceutical composition of claim 53, wherein said compound is an anti-psychotic therapy.

63. The pharmaceutical composition of claim 62, wherein said compound is a therapy for schizophrenia.

64. The pharmaceutical composition of claim 53, wherein said MTHFR allele encodes an MTHFR protein with reduced activity or reduced thermal stability.

65. The pharmaceutical composition of claim 53, wherein said MTHFR allele comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

66. The pharmaceutical composition of claim 53, wherein said MTHFR allele comprises a C/T mutation at position 677 or an A/C mutation at position 1298.

67. The pharmaceutical composition of claim 53, wherein said subject comprises at least two MTHFR mutant alleles.

68. The pharmaceutical composition of claim 67, wherein said mutant MTHFR alleles comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 677, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

69. The pharmaceutical composition of claim 67, wherein said mutant MTHFR alleles comprise at least one of a C/T mutation at position 677 or an A/C mutation at position 1298.

5